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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/078,927	02/19/2002	Thomas Curran	SJ-01-0032	6357

28258 7590 08/22/2005

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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 08/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/078,927	CURRAN ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-8,10,11,13-15,32 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8,10,11,13-15,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Appendices A and B*.

DETAILED ACTION

Status of the Application

[1] A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/16/2005 has been entered.

[2] The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

[3] Claims 1-2, 4-8, 10-11, 13-15, and 32-33 are pending in the application.

[4] Applicants' amendment to the claims, filed 6/16/2005, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[5] Receipt of a paper copy of the sequence listing, filed 4/25/2005, is acknowledged. Receipt of a sequence listing in computer readable form (CRF), a statement of the sameness of the CRF and the paper copy thereof, and a statement that no new matter has been added to the specification by the paper copy of the sequence CRF, all filed 6/16/2005, is acknowledged. It should be noted that applicants have failed to provide a statement directing entry of the paper copy of the sequence listing into the specification. In response to this Office action, applicants are required to provide such statement.

[6] Receipt of a Declaration under 37 CFR 1.132, filed 4/25/2005, is acknowledged.

[7] Applicants' arguments filed 4/25/2005 and 6/16/2005 are acknowledged. Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[8] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Specification/Informalities

[9] The amendment filed 4/25/2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the disclosure of SEQ ID NO:4 in the sequence listing. While the sequence of a disclosed GenBank Accession Number in the specification is considered to be an inherent "incorporation by reference," it is noted that the sequence of GenBank Accession Number 1771281 is not the sequence of SEQ ID NO:4, but instead appears to be a nucleic acid encoding SEQ ID NO:4. Even assuming *arguendo* GenBank Accession Number 1771281 is the sequence of SEQ ID NO:4, there is no evidence of record, *e.g.,* a statement by applicants' representative, that the sequence of SEQ ID NO:4 was identical to the sequence

of GenBank Accession Number 1771281 at the time of filing of the instant application.

Applicant is required to cancel the new matter in the reply to this Office Action.

[10] 37 CFR 1.821 states, "[w]here the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. Accordingly, the "nucleotide sequence of GenBank Accession number 1171281" as recited in claim 33 should be identified by a sequence identifier.

Claim Rejections - 35 USC § 112, Second Paragraph

[11] Claims 1, 4-8, 10-11, 13-15, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claims 1 (claim(s) 4-6 dependent therefrom), 7-8, 10 (claim(s) 11 and 13-14 dependent therefrom), 15, and 33 are indefinite in the recitation of "Cdk5" and "Dab1" as it is unclear as to the scope of polypeptides that are encompassed by the terms. It is noted that the specification defines "Cdk5" as "a protein with serine/threonine kinase activity that is structurally homologous to the mitotic cyclin dependent kinases (Lew et al., J Biol Chem 267:13383-13390, 1992;

Meyerson et al., EMBO J 11:2909-2917, 1992). Cdk5 proteins include, but are not limited to Cdk5 proteins cloned from human (genbank 4826674), mouse (genbank 6680907), and rat (genbank 203389)" (p. 4, lines 14-18). The specification defines "Dab1" as "an intracellular adapter protein that is phosphorylated by Cdk5 activity and by reelin tyrosine kinase activity. Dab1 proteins include, but are not limited to Dab1 proteins cloned from human (genbank 3288851) and mouse (genbank 1771281)" (p. 4, lines 22-25). However, even in view of these definitions, the scope of polypeptides that are encompassed by the terms remains unclear. It is suggested that applicants clarify the scope of intended "Cdk5" and "Dab1" polypeptides.

RESPONSE TO ARGUMENT: In the response filed 4/25/2005, applicants argue the terms "Cdk5" and "Dab1" were well-known at the time of the invention and a skilled artisan would have recognized the intended scope of polypeptides that are referred to by the terms "Cdk5" and "Dab1," providing a Declaration by co-inventor Curran and sequence alignments of Cdk5 and Dab1 as evidence thereof. Applicants state if the examiner maintains the instant rejection, he should provide scientific rationale or evidentiary support for the assertion that the disclosed Cdk5/Dab1 relationship is "peculiar to a single species." In the response filed 6/16/2005, applicants further argue that the terms "Cdk5" and "Dab1" are "creations of the art" used to denote a class of proteins with features that allow them to be distinguished from other proteins and that based on the prior art, a skilled artisan would be able to a "Cdk5" and "Dab1" protein.

Applicants' argument is not found persuasive. MPEP 2111.01 states, "during examination the USPTO must give claims their broadest reasonable interpretation" and that "the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification." In this case, there is no "clear definition" of the terms "Cdk5" and "Dab1" in the specification and even though the terms "Cdk5" and "Dab1" may have been used in the art at the time of the invention, the definitions of the terms in the specification are not limited to those "Cdk5" and "Dab1" polypeptides that were known in the art at the time of the invention. Consequently, it remains unclear as to the scope of "Cdk5" polypeptides whose kinase activity is being measured and the scope of "Dab1" polypeptides that are used as substrates in measuring the kinase activity.

It should be noted that claims 2 and 32 have not been in included in the instant rejection. The scope of "Dab1" polypeptides in claims 2 and 32 is clear as the claims limit the "Dab1" polypeptide to a specific sequence, namely that of SEQ ID NO:4. Further, the specification discloses that phosphorylation of the Dab1 of SEQ ID NO:4 is Cdk5-specific, *i.e.,* Cdk5 specifically phosphorylates the murine Dab1 of SEQ ID NO:4 (see particularly pp. 19-21) and there is no evidence of record that would suggest otherwise. Further Cdk5 activity is observed only in the adult brain (p. 2, top, Declaration filed 4/25/2005). Thus, by limiting the "Dab1" polypeptide to SEQ ID NO:4, the scope of Cdk5 polypeptides whose activity is measured by virtue of phosphorylation of Dab1 is clear as, based on the evidence of the specification, *only* a "Cdk5" polypeptide has the ability to phosphorylate the Dab1 of SEQ ID NO:4.

[b] Claim 2 limits the Dab1 sequence to that of SEQ ID NO:4. Claim 2, to the extent the claim depends from claim 1 and includes all limitations thereof, is confusing in the recitation of "a serine corresponding to position 491 of SEQ ID NO:4 and a serine corresponding to position 515 of SEQ ID NO:4." It is unclear as to which serine of SEQ ID NO:4 "corresponds" to position 491 or 515 of SEQ ID NO:4. In the interest of advancing prosecution, the examiner has interpreted the claim as meaning that "a serine corresponding to position 491 of SEQ ID NO:4" is serine at position 491 of SEQ ID NO:4 and "a serine corresponding to position 515 of SEQ ID NO:4" is serine at position 515. It is suggested that applicants clarify the meaning of the claim.

[c] Claim 33 is indefinite in the recitation of "GenBank Accession Number 1771281" as it is unclear as to the scope of nucleotide sequences that are encompassed by the phrase. A skilled artisan recognizes that the sequences disclosed in a sequence database are revised over time, as evidenced by the revision history for GenBank Accession Number 1771281 (Appendix A). As such, the nucleotide sequence disclosed in GenBank Accession Number 1771281 may not be the same in future revisions.

RESPONSE TO ARGUMENT: Addressing a similar rejection of claim 32 in a previous Office action, applicants argue in the response filed 4/25/2005 that the rejection has been overcome by amendment to replace the GenBank Accession Number with a sequence identifier corresponding to the sequence disclosed by the GenBank Accession Number. In the response filed 6/16/2005, applicants further argue: 1) none of the revisions to GenBank Accession Number

1771281 have resulted in a change to the sequence; 2) Dab1 is the "official symbol" for the nucleic acid encoding this protein and, according to applicants, "GenBank accession number 1771281" provides a clear description of the murine Dab1 protein; and 3) issued US patents have claims referencing a GenBank Accession Number.

Applicants' argument is not found persuasive. There is no way to know with certainty that the sequence of GenBank Accession Number 1771281 will not change. GenBank Accession Numbers are not static, but can change by revision. For example, the revision history for X76104 (Appendix A), a DAP-kinase polypeptide, shows that the sequence for this polypeptide has changed at least once. As such, the amino acid sequence that is represented by a GenBank Accession Number may change over time. Consequently, the scope of polypeptides referred to by the use of a GenBank Accession Number in a claim is unclear. In response to applicants' argument that issued US patents have claims referencing a GenBank Accession Number, it is noted that each patent application is examined on its merits and the examiner is unfamiliar with the prosecution history of the corresponding patent application.

Claim Rejections - 35 USC § 112, First Paragraph

[12] Claims 1-2, 4-8, 10-11, 13-15, and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of he claimed invention. This is a new matter rejection.

Claims 1 (claim(s) 4-8, 10-11, and 13-15 dependent therefrom), 2, and 32 recite the limitation "SEQ ID NO:4." MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims" and "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description." As a showing of support for the recited limitation, applicants point to p. 4, lines 8-13 of the specification, which states, "'Disabled 1 protein' (Dab1) means an intracellular adapter protein that is phosphorylated by Cdk5 activity and by reelin tyrosine kinase activity. Dab1 proteins include, but are not limited to Dab1 proteins cloned from human (genbank 3288851) and mouse (genbank 1771281)."

In this case, that applicants have disclosed GenBank Accession Number 1771281 in the specification, this is an inherent "incorporation-by-reference" of the sequence disclosed by that accession number. However, as noted above, the sequence of SEQ ID NO:4 is not the same as the sequence of GenBank Accession Number 1771281. Instead, GenBank Accession Number 1771281 appears to be the nucleic acid encoding SEQ ID NO:4. As such, the incorporation of SEQ ID NO:4 into the specification is considered to be new matter.

RESPONSE TO ARGUMENT: The issue of new matter regarding the recitation of "SEQ ID NO:4" was raised in the Advisory Action mailed 5/18/2005. Applicants' arguments in the response filed 6/16/2005 that are relevant to the instant rejection are addressed below. Applicants argue mouse Dab1 is defined at p. 4, lines 22-25 of the specification, which is more than a mere reference and the sequence of Dab1 is well-known and can be identified, and therefore, according to applicants, it need not be disclosed in the specification and is preferably omitted. Applicants argue that the examiner made the suggestion to identify GenBank Accession Number 1771281 by a sequence identifier and now that applicant has made such an amendment, the examiner indicates that the information disclosed by GenBank Accession Number 1771281 raises the issue of new matter.

Applicants' argument is not found persuasive. There is no dispute that GenBank Accession Number 1771281 was known at the time of the invention. Also, it is noted that disclosure of a GenBank Accession Number is considered to be an inherent incorporation by reference. However, as noted above, the sequence of GenBank Accession Number 1771281 is a nucleic acid sequence, not a polypeptide sequence. Even assuming *arguendo* GenBank Accession Number 1771281 disclosed the sequence of SEQ ID NO:4, there is no evidence of record that the information disclosed in GenBank Accession Number 1771281 at the time of filing of the instant application is the same as the polypeptide of SEQ ID NO:4. In response to applicants' argument that applicants are following the examiner's suggestion, it is noted that, in view of the context of the definition

of Dab1 in the specification (p. 4), the examiner made such a suggestion assuming that GenBank Accession Number 1771281 referred to a polypeptide sequence and not a nucleic acid sequence.

[13] Claims 1, 4-8, 10-11, 13-15, and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention.

Claim 1 (claim(s) 4-6 dependent therefrom), 7-8, 10 (claim(s) 11, 13-14, dependent therefrom), 15, and 33 are drawn to a method for detecting Cdk5 activity by determining whether a genus of Dab1 proteins is phosphorylated on a serine corresponding to position 491 of SEQ ID NO:4 or position 515 of SEQ ID NO:4 or the nucleotide sequence of GenBank Accession Number 1771281.

The Court of Appeals for the Federal Circuit has held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional

characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single representative species of the genus of recited Dab1 polypeptides, *i.e.,* human and mouse Dab1 having GenBank Accession Numbers 3288851 and 1771281, respectively. Other than these two representative species of Dab1 polypeptides, the specification fails to disclose any other additional representative species of the genus of recited Dab1 polypeptides, which, according to the specification (p. 4), encompasses any intracellular adapter protein that is phosphorylated by Cdk5 activity and by reelin tyrosine kinase activity. In this case, the species encompassed by the genus are widely variant with respect to their structures. As such, the disclosure of the two representative species of Dab1 polypeptides is insufficient to be representative of the attributes and features of all species encompassed by the recited genus of Dab1 polypeptides.

Given the lack of description of a representative number of polynucleotides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

RESPONSE TO ARGUMENT: In the responses filed 4/25/2005 and 6/16/2005, applicants argue: 1) claim 1 has been amended to recite a serine corresponding to position 491 or 515 of SEQ ID NO:4; 2) "Dab1" polypeptide is well-known in the art; and 3) the sequences of Dab1 are highly conserved.

Applicants' argument is not found persuasive. According to the Courts, "[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398. The examiner acknowledges the amendment to limit the genus of Dab1 polypeptides to those that have a serine corresponding to position 491 or 515 of SEQ ID NO:4. However, while it is acknowledged that this structural feature is common to all members of the genus, this structural feature – being only a single amino acid – does *not* constitute a substantial portion of the genus. As noted above, there is no "clear definition" of the term "Dab1" in the specification and even though the term "Dab1" may have been used in the art at the time of the invention, the definition of the term in the specification is not limited to the "Dab1" polypeptides that were known in the art at the time of the invention, including GenBank Accession Numbers 3288851 and 1771281. As such, in accordance with the definition provided by the specification, the term "Dab1" encompasses the structures of any intracellular adapter protein that is phosphorylated by Cdk5 activity and by reelin tyrosine kinase activity.

[14] Claims 1, 4-8, 10-11, 13-15, and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting Cdk5 activity by determining whether SEQ ID NO:4 is phosphorylated at serine 491 or 515 in a biological sample, does not reasonably provide enablement for a method for detecting activity of any polypeptide considered to be a "Cdk5" polypeptide by determining whether any polypeptide considered to be a "Dab1" polypeptide is phosphorylated on a serine corresponding to position 491 of SEQ ID NO:4 or position 515 of SEQ ID NO:4 or the nucleotide sequence of GenBank Accession Number 1771281.

It is the examiner's position that undue experimentation is required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). MPEP 2164.04 states, "[w]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude

that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." Accordingly, the Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: Claims 1 (claim(s) 4-6 dependent therefrom), 7-8, 10 (claim(s) 11, 13-14, dependent therefrom), 15, and 33 are so broad as to encompass a method for detecting activity of any polypeptide considered to be a "Cdk5" polypeptide by determining whether any polypeptide considered to be a "Dab1" polypeptide is phosphorylated on a serine corresponding to position 491 of SEQ ID NO:4 or position 515 of SEQ ID NO:4 or the nucleotide sequence of GenBank Accession Number 1771281. In this case, the specification at p. 4 broadly defines a "Cdk5" polypeptide as "a protein with serine/threonine kinase activity that is structurally homologous to the mitotic cyclin dependent kinases" and broadly defines a "Dab1" protein as "an intracellular adapter protein that is phosphorylated by Cdk5 activity and by reelin tyrosine kinase activity." Thus, the claims are so broad as to encompass a method for detecting activity of any protein with serine/threonine kinase activity that is structurally homologous to the mitotic cyclin dependent kinases by determining whether any intracellular adapter protein that is phosphorylated by Cdk5 activity and by reelin tyrosine kinase activity is phosphorylated on a serine corresponding to position 491 of SEQ ID NO:4 or position 515 of SEQ ID NO:4 or the nucleotide sequence of GenBank Accession Number 1771281. The enablement provided by the specification is not

commensurate in scope with the claim with regard to broad scope of polypeptides encompassed by the claim. In this case, the specification is enabling only for a method for detecting Cdk5 activity by determining whether SEQ ID NO:4 is phosphorylated at serine 491 or 515 in a biological sample.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: At the time of the invention, the Dab1 polypeptides having GenBank Accession Numbers 3288851 and 1771281 were known in the art. However, as noted above, the claims are not so limited and, in view of the broad scope of proteins that are considered to be "Cdk5" and "Dab1" polypeptides, it is highly unpredictable as to whether detecting phosphorylation of any "intracellular adapter protein that is phosphorylated by Cdk5 activity and by reelin tyrosine kinase activity" on a serine corresponding to position 491 or position 515 of SEQ ID NO:4 will indicate Cdk5 kinase activity. Conversely, in view of the disclosed highly specific nature of Cdk5, it is highly unpredictable as to whether phosphorylation of SEQ ID NO:4 at serine 491 or 515 in a biological sample indicates that any "protein with serine/threonine kinase activity that is structurally homologous to the mitotic cyclin dependent kinases" is active.

The amount of direction provided by the inventor and The existence of working examples: The specification discloses only two working examples of the claimed method, *i.e.*, a method for detecting Cdk5 activity by determining whether SEQ ID NO:4 is phosphorylated at serine 491 or 515 in a biological sample. Besides these working examples, the specification fails to disclose any

guidance for detecting phosphorylation of any "intracellular adapter protein that is phosphorylated by Cdk5 activity and by reelin tyrosine kinase activity" on a serine corresponding to position 491 or position 515 of SEQ ID NO:4 will indicate Cdk5 kinase activity or whether phosphorylation of SEQ ID NO:4 at serine 491 or 515 in a biological sample indicates that any "protein with serine/threonine kinase activity that is structurally homologous to the mitotic cyclin dependent kinases" is active.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: In view of the broad definition of the terms "Cdk5" and "Dab1" as provided in the specification, the experimentation required to screen phosphorylation of all polypeptides that are intracellular adapter proteins that are phosphorylated by Cdk5 activity and by reelin tyrosine kinase activity on a serine corresponding to position 491 or position 515 of SEQ ID NO:4 for those whose that provide an indication of the activity of any "protein with serine/threonine kinase activity that is structurally homologous to the mitotic cyclin dependent kinases" is not routine.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner

reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

RESPONSE TO ARGUMENT: Applicants argue that mouse, rat, and human Cdk5 and Dab1 proteins are highly conserved. Applicants further argue that Wang et al. present evidence that the invention works in the rat. Applicants request that the examiner provide evidence to support the Cdk5/Dab1 relationship would not exist in other species.

Applicants' argument is not found persuasive. In view of applicants' evidence that the rat, mouse, and human Dab1 polypeptides are highly related, each having serines at positions 491 and 515, it would appear that Cdk5 activity can be detected in other species by detecting phosphorylation of the Dab1 polypeptide of SEQ ID NO:4 at serine 491 or 515. However, while one of skill in the art may be able to detect Cdk5 activity in mammalian species besides mice by detecting phosphorylation of the Dab1 polypeptide of SEQ ID NO:4 at serine 491 or 515, the claims are not so limited. In this case, the claims are so broad as to encompass a method for detecting activity of any protein with serine/threonine kinase activity that is structurally homologous to the mitotic cyclin dependent kinases by determining whether any intracellular adapter protein that is phosphorylated by Cdk5 activity and by reelin tyrosine kinase activity is

phosphorylated on a serine corresponding to position 491 or 515 of SEQ ID NO:4. At least for the reasons noted above, undue experimentation is required to make the full scope of the claimed invention.

Conclusion

[15] Status of the claims:

Claims 1-2, 4-8, 10-11, 13-15, and 32-33 are pending.

Claims 1-2, 4-8, 10-11, 13-15, and 32-33 are rejected.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Monday to Friday, 7:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656

NCBI

Sequence Revision History

Revision history for 1771281

GI	Version	Update Date	Status	I	II
1771281	1	Aug 5 2003 7:08 AM	Live	◉	○
1771281	1	Oct 14 2002 5:08 PM	Dead	○	◉
1771281	1	Mar 9 1999 4:57 AM	Dead	○	○
1771281	1	Feb 8 1997 6:14 AM	Dead	○	○
1771281	1	Jan 9 1997 1:01 AM	Dead	○	○

Accession Y08379 was first seen at NCBI on Jan 9 1997 1:01 AM

Appendix B

NCBI

Sequence Revision History

Revision history for X76104

GI	Version	Update Date	Status	I	II
2094872	1	Aug 4 2003 7:22 PM	Live	◉	○
2094872	1	Oct 13 2002 6:12 PM	Dead	○	○
2094872	1	Mar 9 1999 1:52 AM	Dead	○	○
2094872	1	May 14 1997 12:11 PM	Dead	○	○
434846	0	May 28 1996 11:34 PM	Dead	○	◉
434846	0	May 23 1995 6:07 PM	Dead	○	○
434846	0	Feb 27 1995 12:05 AM	Dead	○	○
434846	0	Nov 30 1994 6:03 PM	Dead	○	○
434846	0	Dec 15 1993 12:21 AM	Dead	○	○

Accession X76104.1 was first seen at NCBI on Dec 15 1993 12:21 AM